Self-assembling multifunctional nanostructures for the controlled delivery to cancer cells.

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A significant attention of researchers in nanobiotechnology is being directed toward the problems of targeted drug delivery and the development of effective theranostic nanoagents. The aim of this work was the design and synthesis of multifunctional nanostructures as promising agents for effective diagnostics and targeted therapy of cancer. To create such nanoagents, we have developed new universal ways of nanoparticle biofunctionalisation (with preservation of the orientation and functional activity of the molecules being attached) using self-assembly and genetic engineering approaches. In particular, we have used peptides that bind the solid phase (in this case, the surface of nanoparticles) and high affinity protein pair Barnase-Barstar as a "molecular glue" between the combined components. The design of fusion proteins of one component of this pair (e.g., Barstar) with peptide that binds the surface of nanoparticles and the use of fusion proteins of another component (e.g., Barnase) with recognizing or fluorescent molecules (e.g., antibody or fluorescent protein) makes it possible to obtain universal nanostructures with specified characteristics. We have previously shown that Barnase-Barstar protein pair being incorporated into the inteface between nanoparticles of different nature exhibits suprising resistance to dissassembly under severe conditions (8 M GdmHCl, 8 M Urea, 5 M NaCl, pH 1.5), thus providing very strong bond in any environment. The effectiveness of these approaches was demonstrated both in vitro a cell-free mode and by specific cancer cell labelling using the flow cytometry and our original MPQ-cytometry methods.
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